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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/530,451

10/04/2005

Frank Giles

ON/4-32719A

3037

1095

7590

02/11/2009

NOVARTIS
CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

EXAMINER

GHALI, ISIS A D

ART UNIT

PAPER NUMBER

1611

MAIL DATE

DELIVERY MODE

02/11/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

<p align="center">Advisory Action Before the Filing of an Appeal Brief</p>	Application No. 10/530,451	Applicant(s) GILES, FRANK	
	Examiner Isis A. Ghali	Art Unit 1611	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 29 January 2009 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☐ The period for reply expires _____ months from the mailing date of the final rejection.
b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☒ The Notice of Appeal was filed on 29 January 2009. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
(a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
(b) ☐ They raise the issue of new matter (see NOTE below);
(c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
(d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☐ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
The status of the claim(s) is (or will be) as follows:
Claim(s) allowed: _____.
Claim(s) objected to: _____.
Claim(s) rejected: _____.
Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:
See Continuation Sheet.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____.
13. ☐ Other: _____.

/Isis A Ghali/
Primary Examiner, Art Unit 1611

Continuation of 11. does NOT place the application in condition for allowance because:

Applicant argues that PTK787 is much weaker inhibitor of b-EGF induced proliferation than of VEGFR induced proliferation as taught by Tille et al. Such information would surely create some doubts in one of ordinary skill about whether PTK787 would have clinically useful b-FGF inhibitor properties. Since the present claims cover the treatment of patients, such doubts are highly relevant to the question of whether one of ordinary skill would have a reasonable expectation of success based on the prior art.

In response to this argument, it is argued that one cannot show obviousness by attacking the references individually wherein the rejection is based on combination of the references. Tille recognized that cell proliferation could be achieved by inhibition of the bFGF pathway or VEGF pathway with the administration of PTK-787, and Barosi reference teaches that "deregulation of the bFGF pathway in primitive hematopoietic stem cells is hypothesized to be a primary event in the abnormal hematopoiesis of AMM", therefore, if one possessed an inhibitor the bFGF pathway, one could effectively treat AMM. Further, a reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including non-preferred embodiments, and the disclosed examples and preferred embodiment do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. *In re Susi*, 440 F.2d 442, 169 USPQ 423 (CCPA 1971).

Applicant argues that in order to reject the present claims under 35 USC 103, the Examiner must demonstrate that the skilled artisan would have a reasonable expectation of success for treating AMM patients with PTK787 based on the disclosures of the prior art. If correct, the alleged disclosures of the references may provide a basis to formulate a reasonable hypothesis relating to the use of PTK787 for the treatment of AMM. However, Applicants assert that pharmaceutical research is a highly unpredictable field, and the references do not provide any disclosure which would lead the skilled artisan to expect that such a hypothesis will actually turn out to be correct when subjected to experimental testing. There must be some objective teaching in the art that gives the skilled artisan a higher level of confidence for any expectation of success to be reasonable.

In response to this argument, it is argued that Tille recognized that cell proliferation could be achieved by inhibition of the bFGF pathway or VEGF pathway with the administration of PTK-787, and Barosi reference teaches that "deregulation of the bFGF pathway in primitive hematopoietic stem cells is hypothesized to be a primary event in the abnormal hematopoiesis of AMM.", therefore, if one possessed an inhibitor the bFGF pathway, one could effectively treat AMM. Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention to treat AMM using PTK787 as it was suggested by Tille and because Barosi teaches that deregulation of b-FGF pathway in primitive hematopoietic stem cell is hypothesized to be a primary event in the abnormal hematopoiesis of AMM. One would have reasonably expected effectively treating AMM by elements that inhibit bFGF pathway. It has been held that "When a patent simply arranges old elements with each performing the same function it had been known to perform and yields no more than one would expect from such an arrangement, the combination is obvious." *KSR Int 'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1740 (2007) (quoting *Sakraida v. AG Pro, Inc.*, 425 U.S. 273,282 (1976)). "When the question is whether a patent claiming the combination of elements of prior art is obvious," the relevant question is "whether the improvement is more than the predictable use of prior art elements according to their established functions." In addition, "To determine whether there was an apparent reason to combine the known elements in the way a patent claims, it will often be necessary to look to interrelated teachings of multiple patents; to the effects of demands known to the design community or present in the marketplace; and to the background knowledge possessed by a person having ordinary skill in the art. To facilitate review, this analysis should be made explicit. But it need not seek out precise teachings directed to the challenged claim's specific subject matter, for a court can consider the inferences and creative steps a person of ordinary skill in the art would employ". Pp. 11-14. *KSR INTERNATIONAL CO. v. TELEFLEXINC. ET AL.* (2007).

It is well established that the claims are given the broadest interpretation during examination. A conclusion of obviousness under 35 U.S.C. 103 (a) does not require absolute predictability, only a reasonable expectation of success; and references are evaluated by what they suggest to one versed in the art, rather than by their specific disclosure. *In re Bozek*, 163 USPQ 545 (CCPA 1969). In the light of the foregoing discussion, the Examiner's ultimate legal conclusion is that the subject matter defined by the claims would have been prima facie obvious within the meaning of 35 U.S.C. 103 (a).

Applicant argues that it is the hindsight use of the present disclosure which provides the information needed for any expectation of success to be reasonable. Therefore, Applicants believe that such hindsight is the basis for the present rejection.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).